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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,619	10/10/2001	Erin Schuetz	44158/244344	8446

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EXAMINER	
JOHANNSEN, DIANA B	

ART UNIT	PAPER NUMBER
1634	

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DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,619	SCHUETZ ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *33-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☒ Claim(s) *5-7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

1. It is noted that the paper and computer readable forms of the Sequence Listing filed February 13, 2004 have been entered.

Election/Restriction

2. Applicant's election with traverse of Group I, claims 1-32, in the Response of April 23, 2003 is acknowledged. The traversal is on the ground(s) that Groups I-III are not novel and unobvious over each other as required by MPEP 802.01, and that because "a search relating to CYP3A5 would identify art relevant to all three groups because any such search will necessarily focus on the CYP3A5 gene sequence and variants thereof," examination of all three groups would not present a serious burden. This is not found persuasive for the following reasons. First, it is again acknowledged that Groups I and II, and I and III, are related as product and process of use. However, because the products of Inventions II and III may be employed in materially different processes (such as nucleic acid sequencing, or methods of detecting CYP3A5 gene homologues), the inventions have been shown to be distinct by the criteria set forth in MPEP 806.05(h). The products of Groups II-III would not only be useful in the methods of Group I, but in a variety of different methods. Further, while the methods of Group I require particular steps and are directed at detection of polymorphisms in particular locations, the products of Groups II and III may be employed in a variety of different methods unrelated to such polymorphisms. A search of Groups II and III would thus require a search for all the particular products encompassed by each group (irrespective of the manner in which such products might be used), while a search of Group I

requires a search for particular polymorphisms and methods in which those polymorphisms are detected to achieve particular objectives. Thus, Groups I, II, and III each require different searches, and further Group I is classified separately from Groups II and III, by virtue of being directed to a different invention having a different classification. Thus, examination of these distinct inventions would in fact pose a serious burden, and restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 33-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the Response of April 23, 2003.

Claim Objections

4. Claims 5-7 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n).

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see, e.g., pages 32, 62, 77). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

6. The use of the trademarks GENBANK, BIGDYE, and QUANTITY ONE has been noted in this application. The trademarks should be capitalized wherever they appear.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Compliance with Sequence Rules

7. The specification contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a) and (a)(2). However, the specification fails to comply with one or more of the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, and further because the specification recites sequences that lack description by the appropriate sequence identifier set forth in the "Sequence Listing" as required by 37 CFR 1.821(d). See, for example, Table 4 as amended, which continues to recite (in the descriptive material at the bottom of the Table) sequences that are not present in the Sequence Listing and which have not been provided with identifiers. Appropriate corrections for compliance are required.

Applicant is requested to return a copy of the attached Notice to Comply with the response to this Office action.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, while the claims refer to Genbank Accession No. AC005020, the specification does not actually recite the sequence that corresponded to Accession No. AC005020 at the time the instant invention was made. As database Accession entries are not fixed, but rather changeable over time, the recitation of this Accession No. in the claims does not convey to one of skill in the art the sequence actually possessed by Applicant at the time the invention was made, the knowledge of which is required to practice the claimed invention. As the sequence of the molecule employed by Applicant is not disclosed, the claims fail to comply with the written description requirement. It is further noted that as the GENBANK Accession No. was not incorporated into the application by reference, amendment of the specification to add the sequence corresponding to Accession No. AC005020 at the time the invention was made would constitute the addition of new matter.

10. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention of each of the claims includes and requires the knowledge of the sequence set forth in GENBANK Accession No. AC005020. However, the specification does not recite the sequence that corresponded to Accession No. AC005020 at the time the instant invention was made. Accordingly, as the sequence is not provided in the specification, and as knowledge of it is required to practice the methods of the claims, one of skill in the art must look to the teachings of the prior art to determine the identity of the sequence of the claims. However, as database Accession entries are not fixed, but rather changeable over time, the knowledge of this Accession No. does not convey to one of skill in the art the sequence actually possessed and employed by Applicant at the time the invention was made. Only Applicant is aware of the actual version of the sequence employed in, e.g., practicing the examples set forth in the specification. Thus, as neither the specification nor the prior art provide the sequence of the molecule actually employed by Applicant, it would require undue experimentation for one of skill in the art to use the claimed invention. Specifically, as no amount of experimentation would be sufficient to allow one of skill to ascertain what version of Accession No. AC005020 was actually employed by Applicant, and as such knowledge is necessary in order that one of skill might be assured of identifying the particular polymorphisms of the claims, the quantity of experimentation required to use the claimed invention is clearly undue.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-32 are indefinite over the recitation of Genbank Accession No. AC005020 therein. As such database entries are subject to updating and modifications that result in the alteration of the sequences set forth therein, the recitation of such an Accession No. in the claims does not provide a clear and definite description of the sequence encompassed by the claims, and thereby renders the claims vague and indefinite.

Claims 1-7 are indefinite because it is unclear whether the claims are drawn to a method for predicting "the level and distribution of CYP3A5 expression" as recited in the preamble of claim 1, or to a method in which the presence of particular nucleotides are predictive of relative expression levels. Thus, the claims are unclear both a) because it is unclear as to whether the claims actually require a step of predicting, and b) whether said predicting relates to both level and distribution of CYP3A5 expression, or merely to relative levels of expression.

Claims 3 and 5-7 are indefinite over the recitation of the limitation "nucleotide 30,597 of Genbank sequence accession no. AC005020 exon 5 of the Cyp3A5 gene" in claim 3. As independent claim 1 (as well as the specification) identifies position 30,597 as being located in exon 7, the recitation of exon 5 in claim 3 renders these claims indefinite. It appears that the recitation of exon 5 is a typographical error. This rejection could be overcome by amending claim 3 to recite "within exon 7" in lieu of "exon 5."

Claims 8-12 are indefinite because it is unclear whether the claims are drawn to a method of "determining the cytochrome P450 3A5 (CYP3A5) genotype and phenotype of an individual," as recited in the preamble of claim 8, or to a method of "analyzing the cytochrome P450 3A5 (CYP3A5) sequence," as recited in the final process step of the claim. It is not clear how the step of "analyzing" relates to or allows one to determine genotype and phenotype, as required by the claim preamble.

Claims 8-12 are indefinite because it is unclear how steps (b) and (c) in claim 8 relate to one another. Specifically, step (c) merely requires "analyzing the cytochrome P450 3A5 (CYP3A5) sequence;" the claim does not refer back, e.g., to a molecule produced in step (b). Accordingly, it is not clear whether step (c) encompasses "analysis" of any part of the CYP3A5 sequence, or whether this method step is intended to require analysis of, e.g., an amplification product produced in step (b).

Claims 10 and 12 are indefinite over the recitation of the term "primer pairs" preceding a single pair of molecules. It is not clear whether the claims are drawn to the particular pair of primers recited (e.g., to SEQ ID NO: 24 and 25, as recited in claim 10), or whether the use of the plural "pairs" is intended to suggest additional molecules. Clarification is required.

Claims 11-12 are indefinite over the recitation of the limitation "the nucleotide 30,597 point mutation" in claim 11 because there is insufficient antecedent basis for this recitation in the claims.

Claims 13-15 are indefinite because it is unclear whether steps (b) and (c) of claim 13 refer to a single amplification, or whether each step requires a separate

amplification. While steps (b) and (c) each require amplifying, step (c) appears to require the same type of amplifying as step (b). Clarification is required.

Claims 16-19 are indefinite over the recitation of the limitation "the PCR product" in step (b)(i) of claim 16 because there is insufficient antecedent basis for this limitation in the claims.

Claims 20-22 are indefinite because it is unclear whether steps (b) and (c) of claim 20 refer to a single amplification, or whether each step requires a separate amplification. While steps (b) and (c) each require amplifying, step (c) appears to require the same type of amplifying as step (b). Further, step (c) refers to a "first round amplified fragment," suggesting that only one step of amplifying is required prior to step (d). Clarification is required.

Similarly, claims 20-22 are indefinite because it is unclear whether steps (d) and (e) of claim 20 refer to a single amplification, or whether each step requires a separate amplification. While steps (d) and (e) each require amplifying, step (e) appears to require the same type of amplifying as step (d). Clarification is required.

Claims 20-22 are indefinite over the recitation of the limitation "the PCR product" in step (d)(i) of claim 20 because there is insufficient antecedent basis for this limitation in the claims.

Claims 23-25 are indefinite because it is unclear whether steps (b) and (c) of claim 23 refer to a single amplification, or whether each step requires a separate amplification. While steps (b) and (c) each require amplifying, step (c) appears to require the same type of amplifying as step (b). Clarification is required.

Claims 26-29 are indefinite over the recitation of the limitation "the PCR product" in step (b)(i) of claim 26 because there is insufficient antecedent basis for this limitation in the claims.

Claims 26-29 are indefinite over the recitation of the limitation "the intron 3 nucleotide 30,597 of Genbank accession no. AC005020" in claim 26. It is noted that a prior recitation in the claim (as well as the teachings of the specification) indicates that nucleotide 30,597 is located in exon 7, not intron 3. It appears that the recitation of intron 3 in the claim is a typographical error.

Claims 30-32 are indefinite because it is unclear whether steps (b) and (c) of claim 30 refer to a single amplification, or whether each step requires a separate amplification. While steps (b) and (c) each require amplifying, step (c) appears to require the same type of amplifying as step (b). Further, step (c) refers to a "first round amplified fragment," suggesting that only one step of amplifying is required prior to step (d). Clarification is required.

Similarly, claims 30-32 are indefinite because it is unclear whether steps (d) and (e) of claim 30 refer to a single amplification, or whether each step requires a separate amplification. While steps (d) and (e) each require amplifying, step (e) appears to require the same type of amplifying as step (d). Clarification is required.

Claims 30-32 are indefinite over the recitation of the limitation "the PCR product" in step (d)(i) of claim 30 because there is insufficient antecedent basis for this limitation in the claims.

Conclusion

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. It is first noted that Applicant is entitled to an effective filing date of March 29, 2001 with respect to the claimed invention. The polymorphisms of the claims are disclosed in Wojnowski et al (WO 02/053775 A2 [7/02; filed 12/01]); however, the U.S. Provisional applications of which Wojnowski et al claims benefit that were filed prior to the effective filing date of the instant application do not disclose these particular polymorphisms. The 30,597 polymorphism is disclosed in Anastasio et al (WO 02/46209 A2 [6/02; filed 12/01]); however, the U.S. Provisional application of which Anastasio et al claims benefit that was filed prior to the effective filing date of the instant application does not disclose this polymorphism. In a reference published subsequent to the effective filing date of the instant application, Kuehl et al (Nature Genetics 27:383-391 [4/2001]) disclose the 22,893 and 30,597 polymorphisms and the effects thereof on CYP3A5 structure and expression.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Diana B. Johannsen
Patent Examiner
April 30, 2004

Application No.: 09/974,619

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [X] 7. The Sequence Listing is incomplete – see Table 4.

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
Technical Assistance.....703-287-0200
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